Remarks

Numerous typographical, grammatical, and publishing errors were found in the published application, US 2002/0119489 A1. The "Amendments to the Specification," shown on pages 2-19 of this response, is a list of errors falling within these categories. No new matter has been added to this application by this amendment.

The Applicants appreciate the Examiner's straightforward comments regarding claim amendments and have amended the claims accordingly. The Examiner has rejected Claims 1 and 2 under 35 USC § 112, second paragraph, as being indefinite because no Tryptophan exists at position 328 of SEQ ID NO:2. As noted by the Examiner, SEQ ID NO:2 includes a 28 amino acid signal sequence such that, in SEQ ID NO:2, the Tryptophan to which the Applicants refer is located at amino acid position 356. Claim 1, and thus its dependent Claim 2, has been amended to change "position 328" to "position 356."

The Examiner has objected to Claim 1 because Tryptophan was misspelled ("Tryptophane"). The spelling of Tryptophan in this claim and throughout the specification has been corrected through this amendment.

The Examiner has rejected Claims 1 and 2 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement because of new matter. In particular, the Examiner rejected the use of the word "about" when describing the beginning of the mature protein in SEQ ID NO:2. The Examiner also rejected the use of the word "about" under 35 USC § 112, second paragraph, as being indefinite. In view of these rejections, the Applicants have amended Claim 1, and thus dependent Claim 2, by deleting the word "about."

Additionally, the Examiner has rejected Claim 2 under 35 USC § 112, second paragraph, as being indefinite, stating that it fails to indicate what is being compared to the butyrylcholinesterase variant. Claim 2 has been amended such that it is consistent with the specification, reciting that the butyrylcholinesterase variant is "compared to human butyrylcholinesterase."

Finally, the Examiner has provisionally rejected Claims 1 and 2 under obviousness-type double patenting over Claims 1 and 8 of copending Application 10/413,432. The

Applicants have amended Claim 1, and thus its dependent Claim 2, such that it comprises the amino acid sequence of SEQ ID NO:2. The Examiner states that SEQ ID NO:52 of the '432 Application has "100% seq id to amino acids 29-602 of seq. Id. 2" of the instant application and "possesses a trp at position 328." The Applicants respectfully provide herein a comparison of the two sequences:

Met Asp Ser Lys Val Thr Ile Ile Cys Ile Arg Phe Leu Phe Trp Phe Leu
-28 -12
Leu Leu Cys Met Leu Ile Gly Lys Ser His Thr Glu Asp Asp Ile Ile Ile
-1 1 6
Ala Thr Lys Asn Gly Lys Val Arg Gly Met Asn Leu Thr Val Phe Gly Gly 23
Thr Val Thr Ala Phe Leu Gly Ile Pro Tyr Ala Gln Pro Pro Leu Gly Arg 40
Leu Arg Phe Lys Lys Pro Gln Ser Leu Thr Lys Trp Ser Asp Ile Trp Asn 57
Ala Thr Lys Tyr Ala Asn Ser Cys Cys Gln Asn Ile Asp Gln Ser Phe Pro 74
Gly Phe His Gly Ser Glu Met Trp Asn Pro Asn Thr Asp Leu Ser Glu Asp 91
Cys Leu Tyr Leu Asn Val Trp Ile Pro Ala Pro Lys Pro Lys Asn Ala Thr 108
Val Leu Ile Trp Ile Tyr Gly Gly Gly Phe Gln Thr Gly Thr Ser Ser Leu 125
His Val Tyr Asp Gly Lys Phe Leu Ala Arg Val Glu Arg Val Ile Val Val 142
Ser Met Asn Tyr Arg Val Gly Ala Leu Gly Phe Leu Ala Leu Pro Gly Asn 159
Pro Glu Ala Pro Gly Asn Met Gly Leu Phe Asp Gln Gln Leu Ala Leu Gln 176
Trp Val Gln Lys Asn Ile Ala Ala Phe Gly Gly Asn Pro Lys Ser Val Thr 193
Leu Phe Gly Glu Ser Ala Gly Ala Ala Ser Val Ser Leu His Leu Leu Ser 210
Pro Gly Ser His Ser Leu Phe Thr Arg Ala Ile Leu Gln Ser Gly Ser ~~Ala~~ 227
Phe Asn Ala Pro Trp Ala Val Thr Ser Leu Tyr Glu Ala Arg Asn Arg Thr 243
227
Leu Asn Leu Ala Lys Leu Thr Gly Cys Ser Arg Glu Asn Glu Thr Glu Ile 260
Ile Lys Cys Leu Arg Asn Lys Asp Pro Gln Glu Ile Leu Leu Asn Glu Ala 277
Phe Val Val Pro Tyr Gly Thr Pro Leu ~~Gly~~ Ser Val Asn Phe Gly Pro Thr 293
287
Val Asp Gly Asp Phe Leu Thr Asp Met Pro Asp Ile Leu Leu Glu Leu Gly 310
Gln Phe Lys Lys Thr Gln Ile Leu Val Gly Val Asn Lys Asp Glu Gly Thr 327

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Trp Phe Leu Val ~~Met~~ Tyr Gly Ala Pro Gly Phe Ser Lys Asp Asn Asn Ser
                332                                                 343
Ile Ile Thr Arg Lys Glu Phe Gln Glu Gly Leu Lys Ile Phe Phe Pro Gly
                                                                    360
Val Ser Glu Phe Gly Lys Glu Ser Ile Leu Phe His Tyr Thr Asp Trp Val
                                                                    377
Asp Asp Gln Arg Pro Glu Asn Tyr Arg Glu Ala Leu Gly Asp Val Val Gly
                                                                    394
Asp Tyr Asn Phe Ile Cys Pro Ala Leu Glu Phe Thr Lys Lys Phe Ser Glu
                                                                    411
Trp Gly Asn Asn Ala Phe Phe Tyr Tyr Phe Glu His Arg Ser Ser Lys Leu
                                                                    428
Pro Trp Pro Glu Trp Met Gly Val Met His Gly Tyr Glu Ile Glu Phe Val
                                                                    445
Phe Gly Leu Pro Leu Glu Arg Arg Asp Asn Tyr Thr Lys Ala Glu Glu Ile
                                                                    462
Leu Ser Arg Ser Ile Val Lys Arg Trp Ala Asn Phe Ala Lys Tyr Gly Asn
                                                                    479
Pro Asn Glu Thr Gln Asn Asn Ser Thr Ser Trp Pro Val Phe Lys Ser Thr
                                                                    496
Glu Gln Lys Tyr Leu Thr Leu Asn Thr Glu Ser Thr Arg Ile Met Thr Lys
                                                                    513
Leu Arg Ala Gln Gln Cys Arg Phe Trp Thr Ser Phe Phe Pro Lys Val Leu
                                                                    530
Glu Met Thr Gly Asn Ile Asp Glu Ala Glu Trp Glu Trp Lys Ala Gly Phe
                                                                    547
His Arg Trp Asn Asn Tyr Met Met Asp Trp Lys Asn Gln Phe Asn Asp Tyr
                                                                    564
Thr Ser Lys Lys Glu Ser Cys Val Gly Leu
                                        574
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The underlined amino acids are amino acids that occur in SEQ ID NO:2 of the instant application; these include the signal sequence (amino acids -28 to -1) and three additional variants (Phe at position 227, Ser at position 287, and Tyr at position 332). The three lined-through amino acids (Ala at position 227, Gly at position 287, and Met at position 332) are amino acids that occur in SEQ ID NO:52 of the '432 Application, but are different amino acids in SEQ ID NO:2 (see above). Thus, the Applicants assert that SEQ ID NO:2 of the instant application and SEQ ID NO:52 of the '432 Application do not share 100% sequence identity from amino acids 29-602 (or 1-574, as shown above). Applicants further assert that this application, as currently amended, does not conflict with copending Application 10/413,432 as obviousness-type double patenting.

In view of the remarks and amendments provided herein, the Applicants respectfully submit that all rejections and objections have been overcome. The Applicants respectfully

request entry of the amendments, consideration of the arguments, and withdrawal of all rejections and objections.

The Applicants urge the Examiner to call the Applicants' agent at (317) 433-3422 if a telephone conversation or office interview would be helpful in expediting the prosecution of this case.

Respectfully submitted,

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